

Appl. No. 09/607,602
Atty.Docket No. 8141
Amdt. Dated January 12, 2007
Response to Office Action Dated July 18, 2006
Customer Number 27752

REMARKS

Claims 2 to 4 and 7 are pending in the present application. No additional claims fee is believed to be due.

Claim 2 has been amended to recite that the present method involves topical oral administration of a H2-antagonist in an amount effective to decrease blood or systemic levels of C-reactive protein and apolipoprotein B, which are elevated in subjects at risk of developing an oral cavity pathogen-induced systemic disease. Support for this amendment may be found in the Specification at pages 8 to 10 under the discussion on health indices or biomarkers for disease states and in Examples 6 and 7 which demonstrate the effects of the present method in decreasing systemic blood levels of C-reactive protein and apolipoprotein B, respectively in subjects who have increased levels of such biomarkers over normal levels. Such increased blood levels of C-reactive protein and apolipoprotein B are among risk factors for systemic diseases including heart disease and stroke.

Rejection of the Claims Under 35 USC §112, 2nd Paragraph.

Claim 2 has also been amended to delete the word "said" in referring to pathogens. This should address the objection to the phrase "said pathogens" as lacking antecedent basis. Applicants respectfully request withdrawal of the rejection under 35 USC §112, 2nd Paragraph.

Rejection of the Claims under 35 USC §102(b)

Claims 2-4 and 7 have been rejected as being anticipated by each of Pan et al. (WO 97/16159) and Singer et al. (US 5,364,616). Claim 2 is rejected as being anticipated by Tsujita et al. (JP 04089428A). It is contended that the presently claimed benefits are inherent in the referenced methods.

It is respectfully submitted that the claims as now presented are novel over the prior art.

As now specified, the claims are directed to a process namely topical administration to the oral cavity of a composition comprising H-2 antagonist(s) in an amount effective to

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decrease or normalize systemic blood levels of C-reactive protein and apolipoprotein B in a specified group of subjects, i.e., those having or at risk of developing systemic diseases induced by the presence of pathogens in the oral cavity. The elevated levels of C-reactive protein and apolipoprotein B are risk factors for development of certain systemic diseases.

Applicants submit there is no evidence in the record to support the Examiner's contention that the referenced methods inherently anticipate the invention of Claims 2 to 4 and 7. A finding of inherency requires that practicing the prior art method would necessarily and inevitably result in the claimed invention, i.e., decreasing systemic blood levels of C-reactive protein and apolipoprotein B and thereby decreasing risk of development of certain systemic diseases. Inherent anticipation must be established by more than mere probabilities or possibilities. In order for a prior art reference to amount to an inherent anticipation of a claim, all the elements of the claim must *necessarily, inevitably and always* result from the prior art disclosure; mere possibilities or probabilities are not sufficient. *In re Oelrich*, 666 F.2d 578, 581, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981), citing *Hansgirk v. Kemmer*, 102 F.2d 212, 214, 40 U.S.P.Q. 665, 667 (C.C.P.A. 1939). "The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient." *Rapoport v. Dement* 254 F.3d 1053, 1063 (Fed Cir. 2001), citing *Cont'l Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749 (Fed. Cir.1991) (emphasis in original). Furthermore, an accidental or unwitting duplication of an invention may not constitute an anticipation. *In re Marshall*, 578 F.2d 301, 304 (Fed Cir. 1978). Thus, in order for Pan, Singer or Tsujita to inherently anticipate the claimed invention, the method described must result in the claimed invention, i.e., decreasing systemic levels C-reactive protein and apolipoprotein B, *each time and every time* the prior art methods are practiced. Given the vagaries of how the prior art methods may be practiced, inherent anticipation of the claimed method has not been established in this record.

In *Marshall* (Id.), the US Court of Customs and Patent Appeals reversed the rejection of Marshall's claims on the grounds of anticipation because no single piece of prior art contained all the material elements of the claims and because the claims described a new and unanticipated use for an existing drug. Marshall's claims were directed to a process for

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controlling weight using an anesthetic drug, oxethazaine, to inhibit release of the pancreatic secretory hormones, secretin and pancreozymin, in order to control weight. The applied art was the *Physician's Desk Reference* (PDR), which taught using drugs containing the anesthetic oxethazaine to inhibit release of the acid-stimulating hormone, gastrin, in order to treat esophagitis, gastritis, peptic ulcer and irritable colon syndrome. There was no disclosure in the PDR of the activity of oxethazaine to inhibit release of the secretory hormones, which activity makes it useful for losing weight. Therefore if a subject ever lost weight by following the PDR teachings it was an unrecognized accident. The CCPA stated:

An accidental or unwitting duplication of an invention cannot constitute an anticipation. In re Felton, 484 F.2d 495, 500, 179 USPQ 295, 298 (CCPA 1973).

As in *Marshall*, none of the applied citations disclose each and every material element of the claim, in particular the biological activity of H2-antagonists administered topically to the oral cavity to decrease the systemic blood levels of C-reactive protein and apolipoprotein B, which results in preventing the development of systemic disease and thus promoting whole body health in subjects having or at risk for systemic diseases associated with increased levels of C-reactive protein and apolipoprotein B. There is no recognition in the cited art of such patient population and even less that the present claimed treatment would benefit such patient population. If practicing the referenced methods decreased the blood levels of C-reactive protein and apolipoprotein B and thereby reduced risk factors for heart disease and promoted systemic health, it would be an accidental duplication of the present invention. It is respectfully submitted that the applied citations do not constitute an anticipation of the present invention.

It is further submitted that a *prima facie* case of inherency has not been established as required under MPEP 2112 and 2131.02 Section III. As stated therein:

"In relying upon the theory of inherency, the examiner must provide a basis in fact and or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art."

Appl. No. 09/607,602
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"The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish that result or characteristic."

To support the finding of inherency, the Examiner reasons that the relationship between the concept of infection causing inflammation at distant sites is not new.

It is respectfully submitted that such conclusion of inherency is based upon improper hindsight reasoning. There is absolutely no teaching in the referenced art relating to the possibility that pathogens in the mouth and bacterial toxins could enter the systemic circulation via the gums, that such entry would prompt systemic inflammatory mechanisms and complications, specifically to elevate blood levels of C-reactive protein and apolipoprotein B, that such events would be risk factors for development of systemic diseases and that topically administering a H2-antagonist in the oral cavity would decrease or normalize such levels of C-reactive protein and apolipoprotein B. As established in the record from the declaration by present inventor Robert E. Singer, Jr. (submitted in the response dated June 24, 2002 to the Office Action dated December 27, 2001), topical treatment of oral tissues with H2 antagonists serves to increase the barrier function of gingival tissues. The series of studies conducted under Mr. Singer's direction demonstrated that topical H2 antagonists enhance the barrier or protective function of gingival tissues thereby preventing oral pathogens and their products from entering into the systemic circulation. Importantly, topical administration of H2 antagonist compositions to the oral cavity serves to decrease abnormally elevated systemic blood levels of C-reactive protein and apolipoprotein B, thereby reducing risk factors and preventing development of certain systemic diseases and promoting systemic or whole body health.

The referenced art teach nothing more than that H2 antagonists are useful in treating and preventing inflammations in the oral cavity such as gingivitis and periodontitis. Nothing is said or even remotely suggested in the references that topically applied H2-antagonists would decrease the blood levels of C-reactive protein and apolipoprotein B. Without the benefit of the present disclosure, it would not be recognized that topical administration of

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H2-antagonists in the oral cavity would have such biological activity and thereby be effective to reduce risk factors for the development of particular systemic diseases.

Conclusion

This response represents an earnest effort to place the present application in proper form and to distinguish the invention as claimed from the applied reference(s). In view of the foregoing, entry of the amendment(s) presented herein, reconsideration of this application, and allowance of the pending claim(s) are respectfully requested.

Respectfully submitted,

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